Institute, for their valuable advice and comments. We would also like to thank the laboratory members of Toyama Chemical Co. Ltd. for supplying the compounds in the study. Finally, we would like to thank Ms. Mary Phillips and Ms. Yumi Fujiuji for preparing the manuscript.

References

Balzarini J (2004) Current status of the non-nucleoside reverse transcriptase inhibitors of human immunodeficiency virus type 1 *Current Topics in Medicinal Chemistry* **4**:921–944.

Burke CJ, Sanyal G, Bruner MW, Ryan JA, LaFemina RL, Robbins HL, Zeft AS, Middaugh CR & Cordingley MG (1992) Structural implications of spectroscopic characterization of a putative zinc finger peptide from HIV-1 integrase. *The Journal of Biological Chemistry* **267**:9639–9644.

Cain BF, Baguley BC & Denny WA (1978) Potential antitumor agents. 28. deoxyribonucleic acid polyintercalating agents. *Journal of Medicinal Chemistry* **21**:658–668.

Carrasco C, Vezin H, Wilson WD, Ren J, Chaires JB & Bailly C (2001) DNA binding properties of the indolocarbazole antitumor drug NB-506. *Anticancer Drug Design* **16**:99–107.

Chun TW, Finzi D, Margolick J, Chadwick K, Schwartz D & Siliciano RF (1995) *In vivo* fate of HIV-1-infected T cells: quantitative analysis of the transition to stable latency. *Nature Medicine* **1**:1284–1290.

Craigie R, Hickman AB & Engelman A (1995) Integrase. in *HIV: A Practical Approach – Volume 2: Biochemistry, Molecular Biology, and Drug Discovery*; pp. 53–71. Edited by J Karn. New York: Oxford University Press.

Dayam R & Neamati N (2003) Small-molecule HIV-1 integrase inhibitors: the 2001–2002 update. *Current Pharmacology Design* **9**:1789–1802.

De Clercq E (1992) HIV inhibitors targeted at the reverse transcriptase. *AIDS Research and Human Retroviruses* **8**:119–134.

Dziegielewski J, Slusarski B, Konitz A, Skladanowski A & Konopa J (2002) Intercalation of imidazoacridinones to DNA and its relevance to cytotoxic and antitumor activity. *Biochemical Pharmacology* **63**:1653–1662.

Engelman A & Craigie R (1992) Identification of conserved amino acid residues critical for human immunodeficiency virus type 1 integrase function *in vitro*. *Journal of Virology* **66**:6361–6369.

Engelman A, Englund G, Orenstein JM, Martin MA & Craigie R (1995) Multiple effects of mutations in human immunodeficiency virus type 1 integrase on viral replication. *Journal of Virology* **69**:2729–2736.

Engelman A, Hickman AB & Craigie R (1994) The core and carboxyl-terminal domains of the integrase protein of human immunodeficiency virus type 1 each contribute to nonspecific DNA binding. *Journal of Virology* **68**:5911–5917.

Facompre M, Carrasco C, Colson P, Houssier C, Chisholm JD, Van Vranken DL & Bailly C (2002) DNA binding and topoisomerase I poisoning activities of novel disaccharide indolocarbazoles. *Molecular Pharmacology* **62**:1215–1227.

Fukui K & Tanaka K (1996) The acridine ring selectively intercalated into a DNA helix at various types of abasic sites: double strand formation and photophysical properties. *Nucleic Acids Research* **24**:3962–3967.

Furusaki A, Hashiba N, Matsumoto T, Hirano A, Iwai Y & Omura S (1978) X-ray crystal structure of staurosporine: a new alkaloid from a Streptomyces strains. *Journal of the Chemical Society Chemical Communications* 800–801.

Furusaki A, Hashiba N, Matsumoto T, Hirano A, Iwai Y & Omura S (1982) The crystal and molecular structure of staurosporine, a new alkaloid from a Streptomyces strains. *Bulletin of the Chemical Society of Japan* **55**:3681–3685.

Goldgur Y, Craigie R, Cohen GH, Fujiwara T, Yoshinaga T, Fujishita T, Sugimoto H, Endo T, Murai H & Davies DR (1999) Structure of the HIV-1 integrase catalytic domain complexed with an inhibitor: a platform for antiviral drug design. *Proceedings of the National Academy of Sciences, USA* **96**:13040–13043.

Grobler JA, Stillmock K, Hu B, Witmer M, Felock P, Espeseth AS, Wolfe A, Egbertson M, Bourgeois M, Melamed J, Wai JS, Young S, Vacca J & Hazuda DJ (2002) Diketo acid inhibitor mechanism and HIV-1 integrase: implications for metal binding in the active site of phosphotransferase enzymes. *Proceedings of the National Academy of Sciences USA* **99**:6661–6666.

Hazuda DJ, Anthony NJ, Gomez RP, Jolly SM, Wai JS, Zhuang L, Fisher TE, Embrey M, Guare JP, Jr., Egbertson MS, Vacca JP, Huff JR, Felock PJ, Witmer MV, Stillmock KA, Danovich R, Grobler J, Miller MD, Espeseth AS, Jin L, Chen IW, Lin JH, Kassahun K, Ellis JD, Wong BK, Xu W, Pearson PG, Schleif WA, Cortese R, Emini E, Summa V, Holloway MK & Young SD (2004) A naphthyridine carboxamide provides evidence for discordant resistance between mechanistically identical inhibitors of HIV-1 integrase. *Proceedings of the National Academy of Sciences USA* **101**:11233–11238.

Hazuda DJ, Felock P, Witmer M, Wolfe A, Stillmock K, Grobler JA, Espeseth A, Gabryelski L, Schleif W, Blau C & Miller MD (2000) Inhibitors of strand transfer that prevent integration and inhibit HIV-1 replication in cells. *Science* **287**:646–650.

Imamichi T (2004) Action of anti-HIV drugs and resistance: reverse transcriptase inhibitors and protease inhibitors. *Current Pharmaceutical Design* **10**:4039–4053.

Johnson AA, Marchand C & Pommier Y (2004) HIV-1 integrase inhibitors: a decade of research and two drugs in clinical trial. *Current Topics in Medicinal Chemistry* **4**:1059–1077.

Khan E, Mack JP, Katz RA, Kulkosky J & Skalka AM (1991) Retroviral integrase domains: DNA binding and the recognition of LTR sequences. *Nucleic Acids Research* **19**:851–860.

Kohl NE, Emini EA, Schleif WA, Davis LJ, Heimbach JC, Dixon RA, Scolnick EM & Sigal IS (1988) Active human immunodeficiency virus protease is required for viral infectivity. *Proceedings of National Academy of Sciences USA* **85**:4686–4690.

LaFemina RL, Schneider CL, Robbins HL, Callahan PL, LeGrow K, Roth E, Schleif WA & Emini EA (1992) Requirement of active human immunodeficiency virus type 1 integrase enzyme for productive infection of human T-lymphoid cells. *Journal of Virology* **66**:7414–7419.

Long BH, Rose WC, Vyas DM, Matson JA & Forenza S (2002) Discovery of antitumor indolocarbazoles: rebeccamycin, NSC 655649, and fluoroindolocarbazoles. *Current Medicinal Chemistry, Anti-Cancer Agents* **2**:255–266.

Manutto A, Kim YS, Schulze E & Pindur U (2002) New indolocarbazoles as antitumour active compounds: evaluation of the target by experimental and theoretical studies. *Pharmazie* **57**:194–197.

Oka S, Kodama M, Takeda H, Tomizuka N & Suzuki H (1986) Staurosporine, a potent platelet aggregation inhibitor form a *Streptomyces* species. *Agricultural and Biological Chemistry* **50**:2723–2727.

Omura S, Iwai Y, Hirano A, Nakagawa A, Awaya J, Tsuchiya H, Takahashi Y & Masuma R (1977) A new alkaloid AM-2282 of *Streptomyces* origin. Taxonomy, fermentation, isolation and preliminary characterization. *The Journal of Antibiotics, Tokyo* **30**:275–282

Pluymers W, Pais G, Van Maele B, Pannecouque C, Fikkert V, Burke TR, Jr., De Clercq E, Witvrouw M, Neamati N & Debyser Z (2002) Inhibition of human immunodeficiency virus type 1 integration by diketo derivatives. *Antimicrobial Agents and Chemotherapy* **46**:3292–3297.

Pommier Y, Marchand C & Neamati N (2000) Retroviral integrase inhibitors year 2000: update and perspectives. *Antiviral Research* **47**:139–148.

Ross WE, Glaubiger D & Kohn KW (1979) Qualitative and quantitative aspects of intercalator-induced DNA strand breaks. *Biochimica et Biophysica Acta* **562**:41–59.

Rucetti FW (1985) Immunopathology associated with human lymphotropic retroviruses. *Survey and Synthesis of Pathology Research* **4**:210–226.

Schauer M & Billich A (1992) The N-terminal region of HIV-1 integrase is required for integration activity, but not for DNA-binding. *Biochemical and Biophysical Research Communications* **185**:874–880.

Sunthitikawinsakul A, Kongkathip N, Kongkathip B, Phontnakhu S, Daly JW, Spande TF, Nimit Y & Rochanaruangrai S (2003) Coumarins and carbazoles from *Clausena excavata* exhibited antimycobacterial and antifungal activities. *Pharm Medica* **69**:155–157.

Tamaoki T, Nomoto H, Takahashi I, Kato Y, Morimoto M & Tomita F (1986) Staurosporine, a potent inhibitor of phospholipid/Ca^{++} dependent protein kinase. *Biochemical and Biophysical Research Communications* **135**:397–402.

Tronchet JM & Seman M (2003) Non-nucleoside inhibitors of HIV-1 reverse transcriptase: from the biology of reverse transcription to molecular design. *Current Topics in Medicinal Chemistry* **3**:1496–1511.

Wilson WD & Jones RL (1982) Interaction of actinomycin D, ethidium, quinacrine, daunorubicin, and tetralysine with DNA 31P NMR chemical shift and relaxation investigation. *Nucleic Acid Research* **10**:1399–1410.

Woerner AM & Marcus-Sekura CJ (1993) Characterization of a DNA binding domain in the C-terminus of HIV-1 integrase by deletion mutagenesis. *Nucleic Acid Research* **21**:3507–3511.

Received 22 August 2005, accepted 27 September 2005